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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/666,205	09/18/2003	Wolfgang Stampfer	HL/95-22634/CIP	8858

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CIBA SPECIALTY CHEMICALS CORPORATION
PATENT DEPARTMENT
540 WHITE PLAINS RD
P O BOX 2005
TARRYTOWN, NY 10591-9005

EXAMINER	
PAK, YONG D	
ART UNIT	**PAPER NUMBER**
1652	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/22/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/666,205	STAMPFER ET AL.	
	Examiner	Art Unit	
	Yong D. Pak	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 December 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *45-50* is/are pending in the application.

4a) Of the above claim(s) *46,48 and 50* is/are withdrawn from consideration.

5)☐ Claim(s) _ is/are allowed.

6)☒ Claim(s) *45, 47 and 49* is/are rejected.

7)☐ Claim(s) _ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This application is a CIP of PCT/EP03/02439.

The amendment filed on December 22, 2006, canceling claims 1-44 and adding claims 45-50, has been entered.

Claims 45-50 are pending. Claims 46, 48 and 50 are withdrawn. Claims 45, 47 and 49 are under consideration.

Election/Restrictions

Newly submitted claims 46, 48 and 50 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: Claims 46, 48 and 50 are drawn to a polynucleotide encoding a polypeptide comprising the amino acid sequence of SEQ ID NO:48 and variants thereof. However, applicants elected Group I, drawn to a polypeptide comprising the amino acid sequence of SEQ ID NO:48 and variants thereof. As discussed in the Restriction Requirement, the polynucleotides of claims 46, 48 and 49 and polypeptides of claims 45, 47 and 49 are patentably distinct inventions for the following reasons. Polypeptides, which are composed of amino acids, and polynucleotides, which are composed of purine and pyrimidine units, are structurally distinct molecules; any relationship between a polynucleotide and polypeptide is dependent upon the information provided by the nucleic acid sequence open reading frame as it corresponds to the primary amino acid sequence of the encoded polypeptide. While the polypeptides of claims 45, 47 and 49 can made by methods using some, but not all, of the polynucleotides of claims 46, 48 and 49, it can also be recovered from a natural source using by biochemical means.

For instance, the polypeptide can be isolated using affinity chromatography. For these reasons, the polypeptides of claims 45, 47 and 49 are patentably distinct from the polynucleotides of claims 46, 48 and 49.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 46, 48 and 50 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Response to Arguments

Applicant's amendment and arguments filed on December 22, 2006, have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Specification

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code, page 43 for example. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Claim Objections

Claims 45, 47 and 49 are objected to because of the following informalities: in line 2, each of the claims recite "containing within its total sequence the amino cid sequence". In order to improve clarity, Examiner suggests amending the phrase as "comprising the amino acid sequence of SEQ ID NO:48", for example.

Claim 45 is objected to because of the following informalities: in lines 2-3, the claim recites "a sequence with up to about 5% of the amino acids in the sequence of SEQ ID NO:48 replaced by different amino acids". It appears that applicants are claiming a variant of the polypeptide of SEQ ID NO:48, wherein 5% of the amino acids are replaced. In order to improve clarity, Examiner suggests amending the phrase as "a variant of said sequence having up to about 5% of the amino acids in the sequence of SEQ ID NO:48 replaced by different amino acids".

Claim 47 is objected to because of the following informalities: in line 3, the phrase "SGAGAADA**9**L/I)R (SEQ ID No. 3)" has a typo, the letter "9". According to the amino acid sequence of SEQ ID No. 3 disclosed in the Sequence Listing, the phrase should recite "SGAGAADA**(**L/I)R (SEQ ID No. 3)". Appropriate correction is required.

Claim 49 is objected to because of the following informalities: in line 1, the word "of" in front of "having alcohol dehydrogenase activity" is unnecessary. Appropriate correction is required.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 47 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 47 is drawn to a polypeptide having alcohol dehydrogenase activity and comprising of SGAGAADA(L/I)R (SEQ ID NO:3). The claims encompass any or all alcohol dehydrogenase obtained from any source, including any or all mutants, recombinants or variants thereof, and comprising the short amino acid sequence of SEQ ID NO:3. The limitation of comprising SEQ ID NO:3 provides no description on the structure of other parts of the alcohol dehydrogenase and amounts to polypeptides having less than 3% sequence identity to an alcohol dehydrogenase of SEQ ID NO:48 disclosed in the instant invention (10/345 amino acids). Therefore, the claims are drawn to a genus comprising alcohol dehydrogenases having any structure, including any or all recombinants, mutants and variants and comprising SGAGAADA(L/I)R (SEQ ID NO:3).

In *University of Calfornia v. Eli Lilly & Co.,* 43 USPQZd 1938, the Court of Appeals for the Federal Circuit has held that "A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, (or) chemical name,' of the claimed subject matter sufficient to distinguish it from other materials". As indicated in MPEP 2163, the

written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show that Applicant was in possession of the claimed genus. In addition, MPEP 2163 states that a representative number of species means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.

The recitation of "alcohol dehydrogenases" fails to provide a sufficient description of the claimed genus of proteins as it merely describes the functional features of the genus without providing any definition of the structural features of the species within the genus. The CAFC in UC California v. Eli Lilly, (43 USPQ2d 1398) stated that: "in claims to genetic material, however a generic statement such as 'vertebrate insulin cDNA' or 'mammalian insulin cDNA,' without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus." Similarly with the claimed genus of "alcohol dehydrogenases"

proteins, the functional definition of the genus does not provide any structural information commonly possessed by members of the genus which distinguish the protein species within the genus from other proteins such that one can visualize or recognize the identity of the members of the genus.

The claims are drawn to alcohol dehydrogenases having any structure, encompass mutants of any or all any or all alcohol dehydrogenase obtained from any source, including any or all mutants, recombinants or variants thereof, and comprising the short amino acid sequence of SEQ ID NO:3. The specification only describes a polypeptide comprising the amino acid sequence of SEQ ID NO:48, which comprises SEQ ID NO:3, and having alcohol dehydrogenase activity. While MPEP 2163 acknowledges that in certain situations "one species adequately supports a genus," it also acknowledges that "[f]or inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus." In view of the widely variant species encompassed by the genus, this one example of a single species is not enough and does not constitute a representative number of species to describe the whole genus of any or all alcohol dehydrogenase obtained from any source, including any or all mutants, recombinants or variants thereof, and comprising the short amino acid sequence of SEQ ID NO:3, and there is no evidence on the record of the relationship between the structure of the alcohol dehydrogenase of SEQ ID NO:48and the structure of any or all variants, recombinant and mutants of any or all alcohol dehydrogenase isolated from any source. Therefore, the specification fails to describe a representative species of the genus comprising polynucleotides having any structure.

Given this lack of additional representative species as encompassed by the claims, applicants have failed to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize applicants were in possession of the claimed invention.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claim 47 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a polypeptide having the amino acid sequence of SEQ ID NO:48, which comprises SEQ ID NO:3, and having alcohol dehydrogenase activity, does not reasonably provide enablement for any polypeptides having alcohol dehydrogenase activity and comprising the short amino acid sequence of SEQ ID NO:3. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required are summarized in In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in

the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

Claim 47 is drawn to a polypeptide having alcohol dehydrogenase activity and comprising of SGAGAADA(L/I)R (SEQ ID NO:3). The claims encompass any or all alcohol dehydrogenase obtained from any source, including any or all mutants, recombinants or variants thereof, and comprising the short amino acid sequence of SEQ ID NO:3. The limitation of comprising SEQ ID NO:3 provides no description on the structure of other parts of the alcohol dehydrogenase and amounts to polypeptides having less than 3% sequence identity to an alcohol dehydrogenase of SEQ ID NO:48 disclosed in the instant invention (10/345 amino acids). Therefore, the claims are drawn to alcohol dehydrogenases having any structure, including any or all recombinants, mutants and variants and comprising SGAGAADA(L/I)R (SEQ ID NO:3). The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of any or all alcohol dehydrogenase obtained from any or all sources, including any or all variants, recombinants and mutants thereof, broadly encompassed by the claims.

Since the amino acid sequence of the protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to a polypeptide having the amino acid

sequence of SEQ ID NO:48, which comprises SGAGAADA(L/I)R (SEQ ID NO:3), and having alcohol dehydrogenase activity. It would require undue experimentation of the skilled artisan to produce any or all alcohol dehydrogenases obtained from any or all sources, including any or all variants, mutants and recombinants thereof, and comprising the amino acid sequence SGAGAADA(L/I)R (SEQ ID NO:3). In view of the great breadth of the claim, amount of experimentation required to make the claimed polypeptides, the lack of guidance, working examples, and unpredictability of the art in predicting function from a polypeptide primary structure, the claimed invention would require undue experimentation. As such, the specification fails to teach one of ordinary skill how to use the full scope of the polypeptides encompassed by the claims.

While enzyme isolation techniques, recombinant and mutagenesis techniques are known, and it is routine in the art to screen for multiple substitutions or multiple modifications as encompassed by the instant claims, the specific amino acid positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass any or all alcohol dehydrogenase obtained from any sources, including any or all variants, recombinants and mutants thereof, and comprising the amino acid sequence SGAGAADA(L/I)R (SEQ ID NO:3)or polypeptides having less than 3% sequence identity with SEQ ID NO:48, because the specification does not establish: (A)

regions of the structure of an alcohol dehydrogenase which may be modified without effecting its activity; (B) the general tolerance of an alcohol dehydrogenase to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid residue with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any or all alcohol dehydrogenase obtained from any source, including any or all variants, recombinants and mutants and any or all variants, mutants and comprising the amino acid sequence SGAGAADA(L/I)R (SEQ ID NO:3). The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of an alcohol dehydrogenase having the desired biological characteristics recited in the claim is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 45, 47 and 49 are rejected under 35 U.S.C. 102(a) as being anticipated by Wang et al.

Claims 45, 47 and 49 are drawn to an alcohol dehydrogenase comprising the amino acid sequence SGAGAADA(L/I)R (SEQ ID NO:3) or comprising the amino acid sequence of SEQ ID NO:48.

Stampfer et al. (form PTO-1449) discloses a recombinant alcohol dehydrogenase obtained from *Rhodococcus ruber* DSM 44541 (page1014-1015). The specification on page 49 teaches that *Rhodococcus ruber* DSM 14855 and *Rhodococcus ruber* DSM 44541 are the same microorganism. Stampfer et al. uses the same method of isolating the enzyme (pages 42-49 of the instant specification and page 1016 of Stampfer et al.) as described in the specification. Therefore, the alcohol dehydrogenase of Stampfer et al. is 100% identical to the alcohol dehydrogenase of SEQ ID NO:48 of the instant invention, and comprises the amino acid sequence of SEQ ID NO:3. The alcohol dehydrogenase of Stampfer et al. inherently possesses the same material structure and functional characteristics as the alcohol dehydrogenase of claim 47 since both alcohol dehydrogenases are obtained from the same source using the same methods. Since the Office does not have facilities for examining and comparing applicant's alcohol dehydrogenase with the alcohol dehydrogenase of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the alcohol dehydrogenase of the prior art does not possess the same material structure and functional characteristics of the claimed alcohol dehydrogenase). See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977)

and *In re Figzgerald* et al., 205 USPQ 594. Examiner notes that the reference of Stampfer et al. was published online on March 15, 2002, before the filing date of applicant's priority document, EP 02 405 204.5, which was filed on March 18, 2002 (See Stampfer et al. – Online Publication Date – cited previously on form PTO-892). Therefore, the reference of Stampfer et al. anticipates claim 47.

In response to the previous Office Action, applicants have traversed the above rejection.

Applicants argue that since Stampfer et al. does not disclose an amino acid sequence of the alcohol dehydrogenase, said enzyme of Stampfer et al. cannot be assumed to be 100% identical to the alcohol dehydrogenase of SEQ ID NO:48 of the invention (which comprises SEQ ID NO:3). Examiner respectfully disagrees. The alcohol dehydrogenase of Stampfer et al. inherently possesses the same material structure and functional characteristics as the alcohol dehydrogenase of claim 47 since both alcohol dehydrogenases are obtained from the same source using the same methods. Since the Office does not have facilities for examining and comparing applicant's alcohol dehydrogenase with the alcohol dehydrogenase of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the alcohol dehydrogenase of the prior art does not possess the same material structure and functional characteristics of the claimed alcohol dehydrogenase). See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Figzgerald* et al., 205 USPQ 594. Further, MPEP 2112 states that "Once a reference teaching product appearing to be substantially identical is made the basis of a rejection, and the Examiner presents evidence or reasoning tending to

show inherency, the burden shifts to the applicant to show an unobvious difference". Since applicants have not shown an unobvious different, the rejection is maintained.

None of the claims are allowable.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yong Pak whose telephone number is 571-272-0935. The examiner can normally be reached 6:30 A.M. to 5:00 P.M. Monday through Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

Yong D. Pak
Patent Examiner 1652

Manjunath Rao
Primary Patent Examiner 1652